## REMARKS

This paper is responsive to the Office Action dated July 16, 2004 (Paper No. 12), which is the second non-final action on the merits of the application.

Applicant gratefully acknowledges the fact that Group I has been rejoined with Group III, and the restriction between species has been with drawn. Applicant is also grateful for withdrawal of the objection to Claim 10 under 37 CFR § 1.75(c), and the withdrawal of previous rejections under 35 USC § 112 ¶¶ 1 and 2, and 35 USC § 103. New rejections have been raised, which are addressed below.

Claims 1-12 and 23-47 were previously pending in the application, and under examination. Further consideration and allowance of the application is respectfully requested.

Interview:

Applicant thanks Examiner Joseph Woitach for the courtesy of an interview with Michael Schiff at the Patent Office on September 2, 2004. Recommendations made by the Examiner have been incorporated into the claim amendments and remarks presented herein. The application is now believed to be in condition for allowance.

Claim amendments:

Several claims have been amended in a manner that does not introduce new matter into the disclosure. The amendments are supported *inter alia* by the claims as previously filed, and lines 12-17 on page 8 of the specification.

Changes in wording are made so as to simplify wording for convenience of the reader. The amendments do not indicate that applicant thereby surrenders any subject matter previously claimed, or their equivalents. The skilled reader will recognize that the cells and cell populations referred to in the claims may be processed and/or undergo alterations that do not substantially change the claimed method, either between or during the steps explicitly referred to. In particular, various steps may involve or be separated by incubation or culturing of the cells, in which the cells are permitted or caused to proliferate. Steps that involve genetically altering undifferentiated cells in a mixed cell population will often (but not necessarily) involve transfection of the cell population as a whole, thus resulting in genetic alteration of both undifferentiated and differentiated cells. It is the genetic



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alteration of the undifferentiated cells that subsequently allows them to be depleted from the population, if such depletion is desired.

Rejection under 35 USC § 112 ¶ 1:

Claims 1-15 and 23-47 stand rejected under § 112 ¶ 1 as not being described in the specification in such a way as to convey that applicants had possession of the invention. Specifically, the Office Action indicates that the claims encompass a variety of stem cells from tissues such as brain, liver, the hematopoietic system, and mesenchymal cells. It states that the specification fails to teach any promoters that could be used in cells isolated from specific tissues.

Applicant respectfully disagrees. The Office Action is correct to infer that the term "stem cells" in the claims as currently presented goes beyond pPS cells made from embryonic tissue. TERT (the limiting component of telomerase activity) and Oct-4 are exemplary promoters for use in this invention (claim 9). Other examples explicitly cited in the text are promoters associated with the Rex1 zinc finger binding protein, and associated with the family of (at least three) SSEA cell surface markers (page 20, lines 3-9).

However, contrary to what is stated in the Office Action, it is *not true* that expression of these markers is limited to pPS cells. In fact, these markers can be characterized as "stemness" genes, more broadly expressed on stem cells generally — i.e., progenitor cells that have the capacity for self renewal, and to produce mature progeny of one or more tissue types. As such, these markers are expressed in a range of stem cells from various tissues for reasons that relate to their function. For example, expression of TERT increases replicative capacity, which feeds into the ability of stem cells for self renewal.

There are a number of publications that demonstrate expression of each of these four marker families in lineage-committed stem cells from various tissues. Applicant has provided copies of some of these publications in an Information Disclosure Statement filed on or about September 28, 2004 under separate cover (specifically, references CA to CZ). A copy of the abstracts for these articles accompanies this Amendment for the convenience of the Examiner.

A summary table is provided below.



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Marker Expression in Stem Cells

| Publication | Marker Expressed | Stem Cell Type |
|---|---|---|
| Abuljadayel et al. Curr. Med. Res. Opin. 19:355, 2003 | Oct-4 | Blood |
| D'Ippolito et al. J. Cell Science 117:2971, 2004 | Oct-4, Rex1 | Bone marrow |
| Dyce et al. Biochem. Biophys Res. Commun. 316:651, 2004 | Oct-4, Stat3 | Neural |
| Forsyth et al., Differentiation 69:188, 2002 | Telomerase | Skin, liver intestine |
| Gammaitoni et al., Blood 103:4440, 2004 | Telomerase | Cord blood |
| Goolsby et al., Proc. Natl. Acad. Sci. USA 100:14926, 2003 | Rex1, Oct-4 | Hematopoietic |
| Hashimoto et al., J. Clin. Invest. 113:243, 2004 | TERT | Bone marrow |
| Hodes et al., Nat. Rev. 2:699, 2002 | Telomerase | Lymphocytes |
| Mattson et al., Meth. Molec. Biol. 198:125, 2002 | TERT | Embryonic, hematopoietic, neural stem cells |
| Moore et al., DNA Cell Biol. 21:443, 2002 | Telomerase | Corneal epithelial stem cells |
| Murasawa et al., Circulation 106:1133, 2002 | TERT | Endothelial |
| Oh et al., Ann. N.Y. Acad. Sci. 1015:182, 2004 | Telomerase | Heart |
| Parsch et al., J. Molec. Med. 82:49, 2004 | Telomerase | Mesenchymal stem cells |
| Planz et al., Prostate Cancer Prostatic Dis. 7:73, 2004 | Telomerase | Epithelial |
| Pochampally et al., Blood 103:1647, 2004 | Telomerase, Oct-4 | Mesenchymal stem cells |
| Prowse et al., Meth. Molec. Biol. 198:137, 2002 | Telomerase | Neural |
| Reim et al., Dev. Cell 6:91, 2004 | Oct-4 | Endoderm |
| Rubin et al., Archives Gerontology Geriatrics 34:275 (2002) | Telomerase | Stem cells generally |
| Seruya et al., Cell Transpl. 13:93, 2004 | Telomerase | Mesenchymal stem cells |
| Swynghedauw et al., Archives des Maladies du Coeur et des Vaisseaux 96:1225, 2003 | Telomerase | Cardiomyocytes |

Marker Expression in Stem Cells

| Publication | Marker Expressed | Stem Cell Type |
|---|---|---|
| Tabilio et al., Brit. J. Haematol. 58:697, 1984 | SSEA-1 | Hematopoietic |
| Tang et al., Science 291:868, 2001 | Telomerase | Oligodendrocytes |
| Tsai et al., Hu. Reprod. 19:1450, 2004 | Oct-4 | Mesenchymal stem cells |
| Villa et al., Exper. Cell Res. 294:559, 2004 | Telomerase | Neural |
| Yui et al., Blood 91:3255, 1998 | Telomerase | Hematopoietic |

Accordingly, the user can practice the invention of claims 1-15 and 23-47 wherein "P" is a promoter driving expression of TERT, Rex1, Oct-4, or a member of the SSEA family, as explicitly referred to in the text — for a variety of stem cell types, including but not limited to pPS cells, hematopoietic cells, nerve cells of various kinds, mesenchymal stem cells, and so on.

More generally, the specification teaches on page 19, line 10 to page 20, line 15 that markers differentially expressed on stem cells can be identified by microarray techniques, and tested for suitability in this invention using promoter-reporter constructs. By testing expression levels in a type of stem cell of particular interest (regardless of origin), in comparison with expression in mature differentiated cells from the same lineage, the reader will identify markers that are either selective for stem cells generally, or for stem cells of the particular tissue type (e.g., *nestin* as a marker for neural cell progenitors). Promoters driving expression of any of these selectively expressed markers can then be tested as described in the specification for suitability in the claimed invention.

By providing the readers with a list of promoters useable in the invention for a variety of stem cells (either pPS cells or otherwise), and by providing the readers with a strategy for obtaining other suitable promoters selective for any type of stem cell, the disclosure demonstrates that the inventors had possession of the full scope of the claimed invention.

Withdrawal of this rejection is respectfully requested.

Rejections under 35 USC § 112 ¶ 2:

Claim 31 stands rejected under § 112 ¶ 2 for reasons of claim wording.

The amendments to the claim are believed to resolve the issue raised. Withdrawal of this rejection is respectfully requested.

Request for further interview

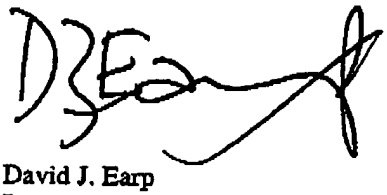
The application is believed to be in condition for allowance, and a prompt Notice of Allowance is requested.

In the event that the Examiner determines that there are other matters to be addressed, applicant hereby requests an interview by telephone.

Fees Due

No fee is believed due with respect to the filing of this amendment. Nevertheless, should the Patent Office determine that an extension of time or any other relief is required for further consideration of this application, applicant hereby petitions for such relief, and authorizes the Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,



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